

REMARKS

Reconsideration of this application, as amended, is respectfully requested. The Applicants wish to draw the Examiner's attention to the applicants' related co-pending applications and issued patents (see Appendix A) directed to nanoparticles and methods of preparation and use thereof. Office actions have already issued on many of the listed cases.

The specification has been amended to update the priority claim as requested by the Examiner. No new matter has been added to the application as a result of this amendment.

Claims 407-420, 423, 424, and 433-444 were pending in this application. Claims 423 and 424 were cancelled and new claims 445-483 were added to further clarify the invention. The new claims are fully supported in the cancelled claims, and thus do not constitute new matter. The new claims are further supported by the specification on page 21, line 3 to page 22, line 22; page 77, line 1 to page 80, line 27; and page 90, line 8 to page 93, line 24. Thus, the new claims do not constitute new matter. Claims 407-420 and 433-483 are now pending in this application.

Turning to the office action, claims 407-420 stand rejected under 35 U.S.C. section 103(a) as being unpatentable over Yguerabide et al. U.S. Patent No. 6,214,560 in view of Sosnowski et al. (U.S. Patent No. 6,518,022). Claims 423 and 424 also stand rejected under 35 U.S.C. section 102(e) as being anticipated by Wohlstadter et al. (U.S. Patent No. 6,066,448). However, claims 423 and 424 were cancelled by amendment and thus the section 102(e) rejection is moot. Finally, claim 415 was rejected under 35 U.S.C. section 112, second paragraph, for indefiniteness. This claim, however, has already been amended and thus the section 112 rejection is moot. The Applicants note, with thanks, that the Examiner had found claims 433-444 to be allowable if presented in independent format, including all of the remaining limitations of the base claim. Applicant respectfully submits, however, that neither Yguerabide nor Sosnowski, alone or in combination, teach or suggest the base claims or any of the remaining pending claims in this application and thus the claims, in their present form, are allowable.

The Examiner had alleged that Yguerabide disclosed a method for detecting target analytes using particulate probes and that Sosnowski disclosed a method for controlling transport, hybridization, and stringency of nucleic acid interactions based on

microelectronic devices. The Examiner believes that based on the combination of Yguerabide's and Sosnowski's teachings, the presently claimed method is obvious. The Applicants traverse this rejection.

As a threshold matter, the Federal Circuit reiterated the manner in which obviousness rejections are to be reviewed. Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, "a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success." *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991), citing *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q. 2d 1529, 1531 (Fed. Cir. 1988). Contrary to the Examiner's position, neither Yguerabide nor Sosnowski, alone or in combination, teach or suggest what the Applicants have done.

Specifically, the Examiner alleged that Yguerabide taught detection and measurement of one or more analytes in a sample using particles of specific composition and size using light scattering. The discussion is found starting in col. 82, line 35, of Yguerabide. Col. 83 provides further discussion regarding particle size and particle binding to a surface. Cols. 77-80 relate to particles and their preparation. Yguerabide, however, is completely silent with respect to any electrode-based method for detecting nucleic acid targets that uses electrically conductive nanoparticle detection probes. In addition, Yguerabide is completely silent with respect to any aging process for preparing nanoparticles. See, for instance, new claims 445 and 450. Nanoparticle-oligonucleotide conjugates prepared by recited process exhibit melting (dehybridization) profiles that are extremely narrow compared to the profiles obtained using the same oligonucleotides not attached to nanoparticles, and exhibit extraordinary selectivity (detection as little as a single base difference) and sensitivity (detecting as little as 10 femtomoles of nucleic acid without amplification) have been obtained using these conjugates in such assays (see particularly Examples 5, 7 and 19) of the present application. These conjugates are surprisingly more stable compared to conjugates made without the recited steps (see, e.g., Example 3 of the present application). The claims recite limitations that are neither taught,

made obvious, or suggested by Yguerabide. Sosnowski adds nothing to Yguerabide that can remedy any of the deficiencies in Yguerabide's teachings.

Sosnowski merely relates to small, micro-fabricated devices for the purpose of moving nucleic acids and other macromolecules to specific locations on the device. The basic principle is that of electrophoresis, i.e. the utilization of an electric field for the main purpose of enhancing hybridization, stringency and control of molecule transport. See Sosnowski at col. 7, line 10. Like Yguerabide, there is nothing in Sosnowski that remotely suggests the capture of a target and nanoparticle probes between two electrodes for the purpose of detection or any electrical method for detection. There is no mention of any electrically conductive nanoparticles or any aging process as recited in the instant claims.

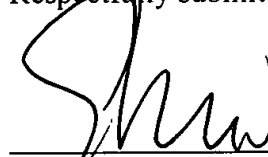
For at least the reasons mentioned above, the Applicants respectfully submit that the combined teachings of Yguerabide with Sosnowski cannot be applied to support section 103(a) rejection of the present and new claims.

In conclusion, the Applicants respectfully submit that the claims in this application are in allowable condition and request a Notice to this effect.

Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. The Examiner is invited to contact the undersigned representative if the Examiner believes that this would be helpful in expediting the prosecution of this application.

Dated: 11/14/03

Respectfully submitted,

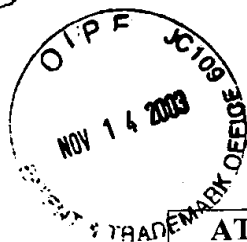


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APPENDIX A

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
00-653-A	U.S. 09/927,777 Filed 8/10/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton, Garamella, Li, Park/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFORE	PENDING
00-713-B1	09/923,625 Filed 8/7/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFOR	PENDING
00-713-C	09/344,667, filed 6/25/99	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFORE	U.S. Patent No. 6,361,944, issued 3/26/02
00-713-I	U.S.S.N 09/603,830 Filed 6/26/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFOR	U.S. Patent No. 6,506,564, issued 1/14/03
00-713-I-1	09/961,949 9/20/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton;	U.S. Patent No. 6,582,921, issued June 24, 2003



ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFOR	
00-713-I-2	09/957,318 9/20/01	See 00-713-I-1	PENDING
00-713-I-3	09/957,313 9/20/01	See 00-713-I-1	U.S. Patent No. 6,645,721, issued 11/11/03
00-713-I-4	09/966,491 9/28/01	See 00-713-I-1	U.S. Patent No. 6,610,491
00-713-I-5	09/966,312 9/28/01	See 00-713-I-1	ALLOWED
00-713-I-6	09/967,409 9/28/01	See 00-713-I-1	PENDING
00-713-I-7	09/974,500 10/10/01	See 00-713-I-1	ALLOWED
00-713-I-8	09/974,007 10/10/01	See 00-713-I-1	PENDING
00-713-I-9	09/973,638 10/10/01	See 00-713-I-1	PENDING
00-713-I-10	09/973,788 10/10/01	See 00-713-I-1	ALLOWED
00-713-I-11	09/975,062 10/11/01	See 00-713-I-1	ALLOWED
00-713-I-12	09/975,376 10/11/01	See 00-713-I-1	PENDING
00-713-I-13	09/975,384 10/11/01	See 00-713-I-1	PENDING
00-713-I-	09/975,498	See 00-713-I-1	ALLOWED

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
14	10/11/01		
00-713-I- 15	09/975,059 11/11/01	See 00-713-I-1	PENDING
00-713-I- 16	09/976,601 10/12/01	See 00-713-I-1	PENDING
00-713-I- 17	09/976,968 10/12/01	See 00-713-I-1	PENDING
00-713-I- 18	09/976,971 10/12/01	See 00-713-I-1	ALLOWED
00-713-I- 19	09/976,863 10/12/01	See 00-713-I-1	PENDING
00-713-I- 20	09/976,577 10/12/01	See 00-713-I-1	ALLOWED
00-713-I- 21	09/976,618 10/12/01	See 00-713-I-1	PENDING
00-713-I- 22	09/981,344 10/15/01	See 00-713-I-1	PENDING
00-713-I- 23	09/976,900 10/12/01	See 00-713-I-1	PENDING
00-713-I- 24	09/976,617 10/12/01	See 00-713-I-1	PENDING
00-713-I- 25	09/976,378 10/12/01	See 00-713-I-1	PENDING
00-713-i- 26	10/410,324 04/10/03	See 00-713-I-1	PENDING
00-713-L	U.S.S.N. 09/693,005 Filed 10/20/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED	U.S. Patent No. 6,495,324, issued 12/17/02

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		THERETO AND USES THEREFORE	
00-713-M	U.S.S.N. 09/693,352 Filed 10/20/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFORE	U.S. Patent No. 6,417,340, issued 7/9/02
00-714-G	U.S. 09/830,620 Filed 8/15/01	Mirkin, Nguyen/ NANOPARTICLES WITH POLYMER SHELLS	PENDING
00-715-A	U.S. 09/760,500 Filed 1/12/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; Garamella, Li/ METHOD OF ATTACHING OLIGONUCLEOTI DES TO NANOPARTICLES AND PRODUCTS PRODUCED THEREBY	ALLOWED
00-1085-A	U.S.S.N. 09/820,279 Filed 3/28/01	Mirkin, Letsinger, etc./ METHOD AND MATERIALS FOR ASSAYING BIOLOGICAL MATERIALS	ALLOWED
00-1086-A	U.S. 09/903,461 Filed 7/11/01	Letsinger, Garimella/ METHOD OF DETECTION BY ENHANCEMENT OF SILVER STAINING	U.S. Patent No. 6,602,669, Filed 8/5/03
01-565-A	USSN 10/125,194 Filed 4/18/02	Mirkin, Nguyen, Watson, Park/ OLIGONUCLEOTI DE-MODIFIED ROMP POLYMERS	PENDING

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		AND CO- POLYMERS	
01-599-A	U.S.S.N. 10/291,291 Filed 11/08/02	Storhoff/NOVEL THIOL-BASED METHOD FOR ATTACHING OLIGONUCLEOTI DES TO NANOPARTICLES	PENDING
01-661-A	U.S.S.N. 10/034,451 Filed 12/28/01	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
01-661-C	U.S.S.N. 10/153,483 Filed 5/22/02	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
01-661-E	U.S.S.N. 10/397,579 3/26/03	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
01-1565-A	U.S.S.N. 10/266,983 Filed 10/08/02	Park, Taton, Mirkin/ARRAY- BASED ELECTRICAL DETECTION OF DNA USING NANOPARTICLE PROBES	PENDING
01-1705-A	U.S.S.N. 10/108,211 Filed 3/27/02	Nam, Park, Mirkin/BIO- BARCODES BASED ON OLIGONUCLEOTI DE-MODIFIED NANOPARTICLES	PENDING
02-338-B	USSN 10/172,428 Filed 6/14/02	Cao, Jin, Nam, Mirkin/MULTI- CHANNEL DETECTION USING NANOPARTICLE	PENDING

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		PROBES WITH RAMAN SPECTROSCOPIC FINGERPRINTS	
02-338-C	10/431,341 5/7/03	Cao, Jin, Nam, Mirkin/MULTICHAN- NEL DETECTION USING NANOPARTICLE PROBES WITH RAMAN SPECTROSCOPIC FINGERPRINTS	PENDING